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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,466	10/27/2006	Maria Teresa Flores	14829-003US1 F/USP288389	5995
26161	7590	07/31/2009	EXAMINER	
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			TON, THAIAN N	
			ART UNIT	PAPER NUMBER
			1632	
			NOTIFICATION DATE	DELIVERY MODE
			07/31/2009	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/564,466	<b>Applicant(s)</b> FLORES ET AL.	
	<b>Examiner</b> Thaian N. Ton	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-22, 25 and 27-33 is/are pending in the application.
- 4a) Of the above claim(s) 1-6, 8-10, 12, 20, 21, 25 and 27-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7, 11, 13-19 and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>1/12/06</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicants' Amendment and Remarks, filed 6/16/09 have been entered. Claims 1-22, 25, 27-33 are pending; claims 29-33 are newly added; claims 1, 2, 7-9, 11-22, 25, 27, 28 are amended; claims 1-6, 8-10, 12, 20, 21, 25, 27-33 are withdrawn; claims 7, 11, 13-19 and 22 are under current examination.

### *Election/Restrictions*

Applicant's election with traverse of Group II (claims 7, 11, 13-19 and 22) in the reply filed on 6/16/09 is acknowledged. The traversal is on the ground(s) that

1) Unity of invention exists because the claims represent one of the categories of invention that are discussed in 37 CFR 1.475. Applicants argue that the claims represent reversibly-immortalized OEG cells and cell lines, pharmaceutical compositions and cell libraries containing the same, and that the claims satisfy 37 CFR 13475(b)(3) and have unity of invention. See pages 7-8 of the Response.

2) The technical feature linking the groups is known in the prior art. Applicants argue that Ramón-Cueto teaches olfactory ensheathing glia (OEG) but the claims as now amended to production of reverse-immortalized human OEG cells. Thus, Applicants argue that reverse-immortalized OEG cells are not the same as the naturally occurring human OEG cells described in Ramón-Cueto, and therefore, the restriction requirement should be withdrawn. See pages 3-7 of the Response.

This is not found persuasive because of the following:

Applicants have amended the claims such that they now read on reverse-immortalized human OEG cells. Thus, the Examiner agrees to the extent that the prior art of Ramón-Cueto does not anticipate or make obvious the instantly amended claims. However, the technical feature of the claims is considered to be

reverse-immortalized human OEG cells, but this technical feature is not considered to be a *special* technical feature, because it does not make a contribution over the prior art of Barnett *et al.* (**Brain**, 123:1581-1588, 2000) when taken with Salmon *et al.* (**Mol. Therapy**, 2(4): 404-414, 2000, IDS) in further view of Halfpenny (**The Lancet Neurology**, 1: 31-40, 2002), which is found below. Thus, given that the technical feature of the claims do not contribute over the prior art, unity of invention is found to be lacking. Additionally, the Examiner notes that 37 CFR 13475(b)(3) is directed to a specific combination of product, process of manufacture, and use of said product. See also, MPEP §1850, which states in part, “When an application includes claims to more than one product, process, or apparatus, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the "main invention" in the claims.” In the instant case, the first category is directed to a process of manufacture, not a product, as set forth in 37 CFR 1.475(b)(3).

With regard to Applicants arguments that no unity of invention rejection was raised by the International Search Authority in connection with PCT/GB2004/003149, the Examiner responds that lack of unity can be determined at any time during prosecution of a national stage application. In particular, 37 CFR 1.499 states, “If the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner.” (Emphasis added). Thus, for at least the reasons set forth above, unity of invention is found to be lacking.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 8-10, 12, 20, 21, 25, 27-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Newly added claims 29-33 are directed to non-elected groups. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/16/09.

***Information Disclosure Statement***

Applicants' IDS, filed 1/12/06, has been considered.

***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The UK Patent Application, 0316882.0 has been entered.

***Claim Objections***

Claim 7 is objected to because Applicants have elected "a population of reverse-immortalized human OEG cells produced by the method of claim 1" as recited in claim 7. Claim 1 is not under current examination, therefore, it is suggested that Applicants amend the examined claim 7 to incorporate the pertinent limitations in withdrawn, non-elected claim 1. Claim 11 is similarly objected to because it depends from non-elected claim 9. Appropriate correction is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7, 11, 13-17, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnett *et al.* (**Brain**, 123:1581-1588, 2000) when taken with Salmon *et al.* (**Mol. Therapy**, 2(4): 404-414, 2000, IDS) in further view of Halfpenny (**The Lancet Neurology**, 1: 31-40, 2002).

Barnett teach the isolation and identification of human olfactory ensheathing glial cells (p. 1582, col. 1, Isolation and Culturing of human OECs). Barnett teach the purification of the human OECs (p. 158, 2nd col., Purification of hOEC using L-NGFr and Magnetic Beads). Barnett teach that cells are capable of remyelinating persistently demyelinated CNS axons following transplantation into rat spinal cord (Abstract).

Barnett do not teach that their cells are reversibly immortalized. However, prior to the time of the claimed invention, Salmon teach the reversible immortalization of human primary cells by lentivector-mediated transfer. In particular, Salmon teach utilizing a vector comprising the SV40 large T (Tag) oncogene (Abstract). Regarding claim 13, Salmon further teach using vectors that contain two LoxP-containing excisable lentiviral vectors that express TAg. (Figure 1 and p. 408, 1st col., 1st ¶). Regarding claim 14, Salmon teach that the immortalization is reversible (p. 411, col. 2, Discussion). Regarding claim 15,

Salmon teach using GFP as a marker gene (p. 409, col. 1, Design of Excisable Lentiviral Vectors). Regarding claims 16-17, Salmon teach that the vector contains thymidine kinase (p. 409, col. 1, Design of Excisable Lentiviral Vectors) and that the cells are sensitive to ganciclovir (p. 409, col. 1, Excision of the Transgene and Conditional Ablation of Unexcised Cells).

Accordingly, in view of the combined art of Barnett and Salmon, it would have been obvious for the ordinary skilled artisan to modify the OEG cells, taught by Barnett, to produce reversibly-immortalized OEG cells, utilizing the methods of Salmon, with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to produce reversibly-immortalized OEG cells in order to produce a large number of therapeutic cells for transplantation, as suggested by Salmon (p. 404, Introduction) and further specifically suggested by Halfpenny who teach immortalized cell lines would provide sufficient numbers of cells for transplantation, which could yield large numbers of appropriate cells in homogeneity. See p. 34, col. 2, Immortalised Cell Lines.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 18 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnett *et al.* (**Brain**, 123:1581-1588, 2000) when taken with Salmon *et al.* (**Mol. Therapy**, 2(4): 404-414, 2000, IDS) in further view of Halfpenny (**The Lancet Neurology**, 1: 31-40, 2002) as applied to claims 7, 11, 13-17, 19 above, and further in view of Franklin *et al.* (**Glia**, 17: 217-224, 1996).

Barnett, Salmon and Halfpenny are discussed above. They do not specifically teach an OEG cell line. However, prior to the time of the claimed invention, Franklin teach the generation of olfactory bulb ensheathing cell lines (p. 218, col. 1, Materials and Methods, Construction of the tsT OBEC Cell line and verification of Clonality).

Accordingly, in view of the combined teachings, it would have been obvious for one of ordinary skill in the art to utilize the teachings of Barnett, Salmon and Halfpenny, to produce a reverse-immortalized human OEG cell culture, and then utilize the teachings of Franklin, in order to produce a clonal reverse-immortalized human OEG cell line, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to make a cell line in view of Franklin's teachings, who state that, "The reason for using a cell line rather than cells derived from primary culture is that it is difficult to obtain pure populations of the latter that are free from any contaminant phenotype." See p. 218, col. 1, 1<sup>st</sup> full ¶.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.



***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/  
Primary Examiner, Art Unit 1632